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Patterns of healthcare utilization in patients with generalized anxiety disorder in general practice in Germany

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ABSTRACT – *Background and Objectives*: To describe patterns of healthcare utilization among patients with generalized anxiety disorder (GAD) in general practitioner (GP) settings in Germany.

Methods: Using a large computerized database with information from GP practices across Germany, we identified all patients, aged ≥ 18 years, with diagnoses of, or prescriptions for, GAD (ICD-10 diagnosis code F41.1) between October 1, 2003 and September 30, 2004 ("GAD patients"). We also constituted an age- and sex-matched comparison group, consisting of randomly selected patients without any GP encounters or prescriptions for anxiety or depression (a common comorbidity in GAD) during the same period. GAD patients were then compared to those in the matched comparison group over the one-year study period.

Results: The study sample consisted of 3340 GAD patients and an equal number of matched comparators. Mean age was 53.2 years; 66.3% were women. Over the 12-month study period, GAD patients were more likely than matched comparators to have encounters for various comorbidities, including sleep disorders (odds ratio [OR] = 6.75 [95% CI = 5.31, 8.57]), substance abuse disorders (3.91 [2.89, 5.28]), and digestive system disorders (2.62 [2.36, 2.91]) (all $p < 0.01$). GAD patients averaged 5.6 more GP encounters (10.5 [SD = 8.8] vs 4.9 [5.7] for comparison group) and 1.4 more specialist referrals (2.3 [2.9] vs 0.9 [1.7]) (both $p < 0.01$). Only 58.3% of GAD patients received some type of psychotropic medication (i.e., benzodiazepines, antidepressants, and/or sedatives/hypnotics).

Conclusions: Patients with GAD in GP practices in Germany have more clinically recognized comorbidities and higher levels of healthcare utilization than patients without anxiety or depression.

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Introduction

Generalized anxiety disorder (GAD) is a chronic condition characterized by persistent worry or anxiety that occurs more days than not over a period of at least 6 months[1], and is difficult to diagnose because of differing clinical presentations and the common occurrence of comorbid somatic diseases and/or mental disorders. Lifetime prevalence of GAD has been estimated to be 4%-6%[2]; one-year prevalence is about 2%[3,4]. GAD occurs infrequently among persons aged < 35 years, and is two to three times more common among women[3]. It is the most common anxiety disorder among patients presenting to primary care physicians[5,6], and is probably overrepresented in primary care settings, with point prevalence estimates at least 2-3 times higher than that noted in the community[6,7].

Most GAD patients experience other mental disorders during their lifetimes, most often major depressive disorder (MDD)[8-10]. One review estimated that over one year, 59% of patients with GAD had comorbid MDD, 71% had some form of depressive disorder, 29% had social phobia, 48% had a somatoform disorder, and 6% had alcohol abuse/dependence[3]. GAD patients also often have other comorbidities, including peptic ulcer disease, diabetes, and irritable bowel syndrome; cardiac and other somatic symptoms are also common[11-19].

The impact of GAD on health-related quality of life and role functioning has been reported to be greater than that of MDD[4]. Also, because of comorbidities and frequent somatic complaints, GAD patients have been reported to have comparatively high levels of healthcare utilization and costs[20,21]. Detailed information on patterns of healthcare utilization among GAD patients is limited, however. One small survey-based study at community clinics in Canada reported that patients (n = 219) who screened positive for GAD averaged 5.3 medical visits annually versus 3.4 visits for other patients[22]. GAD has been associated with a twofold increase in visits to primary care physicians as compared with patients without GAD, with or without depression, but with similar sociodemographic characteristics and chronic physical conditions[20,23]. Among US patients with new episodes of anxiety (any type), mean total annual medical care costs have been reported to average $6,475, or $2,138 more than patients without anxiety[24]. One European study that used a health-economics model estimated that the mean total annual cost per case of GAD was €1,804; corresponding estimates were €350 for obsessive-compulsive disorder, €967 for panic disorder, €937 for social phobia, and €3,826 for depression[25].

In this study, we examine the characteristics of patients with GAD in GP settings in Germany –including their comorbidities, medica-

tion use, and use of healthcare services– and compare them with those of age- and sex-matched patients without evidence of GAD also under GP care. This examination should improve knowledge of "real-world" patterns of healthcare utilization among patients with GAD under the care of GPs.

Methods

Database

Data were obtained from the IMS Medi-Plus - Disease Analyzer database, which provides patient-level information on diagnoses and treatments, and is comprised of about 4.2 million patient records and 75 million prescriptions over a 10-year period. The database is compiled by sampling from approximately 900 GP practices throughout Germany and is designed to be representative of the general population in Germany. All patient identifiers in the database are fully encrypted.

Information in the database includes date of service, diagnoses (in ICD-10 format), actions taken (e.g., referrals to other providers [i.e., specialists], dispensing of sick notes [physician-excused absences from work]), and medications dispensed, including associated diagnoses. Selected demographic information is also available. All patient-level data can be arrayed chronologically to provide a detailed, longitudinal profile of all medical and pharmacy services rendered by participating GPs.

Sample Selection

The study sample consisted of all patients, aged ≥ 18 years, with any GP visits resulting in a diagnosis of –or prescription for– GAD (ICD-10 diagnosis code F41.1) between October 1, 2003 and September 30, 2004 ("study period") (ICD-10 diagnoses were used in lieu of criteria set forth in the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition [DSM-IV], as information on the latter was not available in the database). A comparison group also was constituted, consisting of randomly selected patients without any GP encounters or prescriptions for anxiety (e.g., panic disorder, obsessive-compulsive disorder, post-traumatic stress disorder, phobias, GAD) or depressive disorders (e.g., dysthymic disorder, adjustment disorder with depression, bipolar depression, major depressive disorder) during the same period, matched 1:1 to GAD patients based on age (within 5 years) and sex. Comparison group patients were selected from among all patients without evidence of anxiety or depression (rather than anxiety alone), as GAD patients often receive diagnoses of other anxiety or mood disorders (sometimes in lieu of a GAD diagnosis). All GP encounters were compiled for all GAD and comparison group patients over the study period.

Measures

We examined the prevalence of selected comorbidities over the 12-month study period, including: (1) neoplasms; (2) circulatory system disorders; (3) digestive system disorders; (4) somatoform disorders; (5) substance abuse disorders; and (6) sleep disorders. Patients were deemed to have these conditions if they had *any* encounters during the study period with the corresponding diagnosis code(s).

We examined the number of patients receiving selected medications during the study period, with particular focus on psychotropic medications (i.e., benzodiazepines, antide-

pressants, sedatives/hypnotics); we also examined the use of healthcare services (i.e., GP visits, referrals to other healthcare providers, hospitalizations) and receipt of sick notes (physician-excused absences from work [diagnosis unspecified]). These measures were examined in terms of the number of patients receiving each service, and the total number of times it was rendered.

Analyses

Use of prescription medication was examined in terms of the numbers of patients who received various medications and the numbers of prescriptions thereof. As many of the measures of interest were not normally distributed (e.g., number of prescriptions received, number of visits), statistical significance of differences between GAD patients and matched comparators was assessed using Wilcoxon signed-rank tests for continuous measures, and McNemar's or Bowker's tests, as appropriate, for differences in categorical measures. All analyses were conducted using PC-SAS® v.8.4[26].

Results

The study sample consisted of 6680 patients-3340 with GAD, and an equal number of matched comparators. Mean (±SD) age was 53.2 (17.7) years; 66.3% were women.

One-fifth of GAD patients had evidence of other anxiety disorders during the study period, and 28.8% had comorbid depression; 44.6% had comorbid anxiety and/or depression (Table I) (comparison group patients, by definition, could not have these disorders). GAD patients were more likely than matched comparators to have other mental disorders, including neurasthenia, sleep disorders, and substance abuse disorders (all $p < 0.01$); they also were more likely to have comorbidities, including digestive system disorders and circulatory system disorders (both $p < 0.01$).

During the study period, 58.3% of GAD patients received one or more psychotropic medications; 30.8% received benzodiazepines, and 37.2% received antidepressants. GAD patients were more likely than matched

Table I
Prevalence of concurrent somatic diseases and mental disorders among GAD patients and age- and sex-matched comparison group*

Comorbid Condition	GAD Patients (N = 3,340)	Comparison Group (N = 3,340)	OR (95% CI)	*P*-Value
Psychiatric disorders				
Anxiety disorders				
Panic disorder	144 (4.3)	–	–	–
OCD	13 (0.4)	–	–	–
PTSD	7 (0.2)	–	–	–
Phobias				
Social phobia	4 (0.1)	–	–	–
Agoraphobia	11 (0.3)	–	–	–
All other phobias	53 (1.6)	–	–	–
Any phobia	67 (2.0)	–	–	–
GAD	3,340 (100.0)	–	–	–
Other anxiety disorder	634 (19.0)	–	–	–
Any anxiety disorder	3,340 (100.0)	–	–	–

Table I (continue)*

Comorbid Condition	GAD Patients (N = 3,340)	Comparison Group (N = 3,340)	OR (95% CI)	*P*-Value
Depression disorders				
Dysthymic disorder	44 (1.3)	–	–	–
Adjustment disorder with depression	24 (0.7)	–	–	–
Bipolar depression	1 (0.0)	–	–	–
MDD	107 (3.2)	–	–	–
Unspecified depression	856 (25.6)	–	–	–
Any depression	962 (28.8)	–	–	–
Substance use disorders	205 (6.1)	55 (1.6)	3.91 (2.89, 5.28)	< 0.01
Sleep disorders	485 (14.5)	82 (2.5)	6.75 (5.31, 8.57)	< 0.01
Somatoform disorders	547 (16.4)	101 (3.0)	6.28 (5.05, 7.81)	< 0.01
Neurasthenia	218 (6.5)	32 (1.0)	7.22 (4.96, 10.49)	< 0.01
Number of				
Concurrent anxiety disorders**				
0	2,532 (75,8)	–	–	–
1	752 (22,5)	–	–	–
2	54 (1,6)	–	–	–
≥ 3	2 (0,1)	–	–	–
Concurrent depression disorders				
0	2,378 (71,2)	–	–	–
1	894 (26,8)	–	–	–
2	66 (2,0)	–	–	–
≥ 3	2 (0,1)	–	–	–
Concurrent anxiety and/or depression disorders**				
0	1,852 (55,4)	–	–	–
1	1,124 (33,7)	–	–	–
2	323 (9,7)	–	–	–
≥ 3	41 (1,2)	–	–	–
Any of above				
Other disorders				
Circulatory system disorders	1,990 (59.6)	1,339 (40.1)	2.20 (2.00, 2.43)	< 0.01
Musculoskeletal system disorders	1,844 (55.2)	1,295 (38.8)	1.95 (1.77, 2.15)	< 0.01
Symptoms, signs, ill-defined conditions	1,729 (51.8)	891 (26.7)	2.95 (2.66, 3.27)	< 0.01
Digestive system disorders	1,519 (45.5)	806 (24.1)	2.62 (2.36, 2.91)	< 0.01
Respiratory system disorders	1,460 (43.7)	1,005 (30.1)	1.80 (1.63, 2.00)	< 0.01
Eyes, nose, and throat	1,004 (30.1)	717 (21.5)	1.57 (1.41, 1.76)	< 0.01
Painful neuropathic disorders	822 (24.6)	402 (12.0)	2.39 (2.09, 2.72)	< 0.01
Diabetes	463 (13.9)	316 (9.5)	1.54 (1.32, 1.79)	< 0.01
Anemia and other blood/ antibody disorders	388 (11.6)	155 (4.6)	2.70 (2.23, 3.28)	< 0.01
Neoplasms	328 (9.8)	198 (5.9)	1.73 (1.44, 2.08)	< 0.01

*All values represent number (%) of patients with encounters resulting in any of the above-listed diagnoses over a 12-month period.
**Excluding GAD.
GAD: Generalized anxiety disorder.

comparators to have received other medications, including cardiovascular drugs and opioids (both short- and long-acting formulations) (both $p < 0.01$) (Table II). GAD patients averaged 4.3 more prescriptions (7.8 [7.8] vs 3.5 [5.0] for the comparison group); excluding psychotropic medications, corresponding numbers were 9.5 (12.4) and 4.8 (8.3) respectively (both $p < 0.01$) (Figure).

Table II
Number of GAD patients and patients in age- and sex-matched comparison group receiving various medications*

Medication Type	GAD Patients (N = 3,340)	Total Comparison Group (N = 3,340)	OR (95% CI)	*P*-Value
Cardiovascular system	1,566 (46.9)	1,048 (31.4)	1.93 (1.75, 2.13)	< 0.01
Alimentary tract and metabolism	1,380 (41.3)	852 (25.5)	2.06 (1.85, 2.28)	< 0.01
NSAIDs & COX-2 inhibitors	1,348 (40.4)	828 (24.8)	2.05 (1.85, 2.28)	< 0.01
Antidepressants	1,241 (37.2)	0 (0.0)	---	< 0.01
Benzodiazepines	1,028 (30.8)	54 (1.6)	27.06 (20.47, 35.76)	< 0.01
Systemic general anti-infectives	873 (26.1)	673 (20.1)	1.40 (1.25, 1.57)	< 0.01
Systemic hormonal preparations	645 (19.3)	423 (12.7)	1.65 (1.44, 1.89)	< 0.01
Dermatologicals	560 (16.8)	375 (11.2)	1.59 (1.38, 1.83)	< 0.01
Blood and blood forming organs	535 (16.0)	311 (9.3)	1.86 (1.60, 2.16)	< 0.01
Genito-urinary system and sex hormones	385 (11.5)	222 (6.6)	1.83 (1.54, 2.17)	< 0.01
Antipsychotics	369 (11.0)	32 (1.0)	12.84 (8.92, 18.49)	< 0.01
Sedatives & hypnotics	368 (11.0)	65 (1.9)	6.24 (4.77, 8.16)	< 0.01
Opioids	264 (7.9)	115 (3.4)	2.41 (1.92, 3.01)	< 0.01
Corticosteroids	129 (3.9)	74 (2.2)	1.77 (1.33, 2.37)	< 0.01
Antiepileptics	108 (3.2)	30 (0.9)	3.69 (2.45, 5.54)	< 0.01
Muscle relaxants	63 (1.9)	42 (1.3)	1.51 (1.02, 2.24)	0.04
Anti-migraine medications	65 (1.9)	35 (1.0)	1.87 (1.24, 2.83)	< 0.01
Antineoplastic and immunomodulating agents	38 (1.1)	30 (0.9)	1.27 (0.78, 2.05)	0.33
Any of above	2,981 (89.3)	2,295 (68.7)	3.78 (3.31, 4.31)	< 0.01
None of above	359 (10.7)	1,045 (31.3)	0.26 (0.23, 0.30)	< 0.01
Number of psychotropic medications received**				
0	1,393 (41.7)	3,222 (96.5)	0.03 (0.02, 0.03)	---
1	1,206 (36.1)	113 (3.4)	16.14 (13.21, 19.72)	---
2	477 (14.3)	5 (0.1)	111.13 (45.98, 268.60)	---
≥ 3	264 (7.9)	0 (0.0)	---	---
Any of above	1,947 (58.3)	118 (3.5)	38.16 (31.37, 46.44)	< 0.01

*All values represent number (%) of patients receiving the above-listed medications over a 12-month period.
**Consists of antidepressants, benzodiazepines, sedatives & hypnotics
GAD: Generalized anxiety disorder; NSAID: Nonsteroidal anti-inflammatory drug; COX: Cyclo-oxygenase

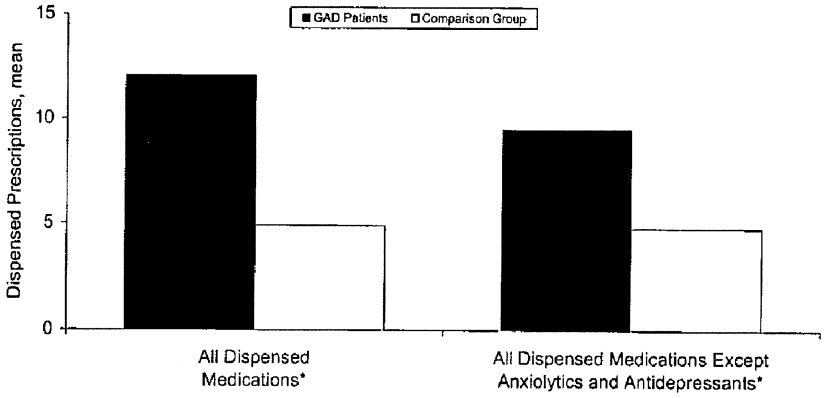

Figure. Mean number of dispensed prescriptions among GAD patients and patients in age- and sex-matched comparison group
*Differences between GAD patients and comparison group were significant ($p < 0.01$)

Use of psychotropic medications by GAD patients increased with age: 51.7% among those aged < 45 years, 57.8% among those aged 45-64 years, and 66.7% among those aged ≥ 65 years ($p < 0.01$); there also was a statistically significant difference by gender (60.6% among women vs 53.7% among men [$p < 0.01$]).

GAD patients averaged 5.6 additional GP visits, 1.4 more referrals, 0.1 additional hospitalizations, and 0.5 more sick notes (physician-excused absences from work) than matched comparators over 12 months (all $p < 0.01$) (Table III).

Table III
Numbers of provider visits, referrals, hospitalizations, and sick notes among GAD patients and patients in age- and sex-matched comparison group*

		GAD Patients (N = 3,340)	Comparison Group (N = 3,340)	*P*-Value
GP visits	0	0 (0.0)	0 (0.0)	
	1	281 (8.4)	1,094 (32.8)	
	2	258 (7.7)	482 (14.4)	
	3-4	426 (12.8)	565 (16.9)	< 0.01
	5-6	371 (11.1)	362 (10.8)	
	7-9	537 (16.1)	349 (10.4)	
	10-13	530 (15.9)	237 (7.1)	
	> 13	937 (28.1)	251 (7.5)	
	Mean (SD)	10.5 (8.8)	4.9 (5.7)	< 0.01
	Median	8	3	
	Minimum	1	1	
	Maximum	75	53	
Referrals	0	1,096 (32.8)	2,018 (60.4)	
	1	659 (19.7)	670 (20.1)	
	2	437 (13.1)	271 (8.1)	< 0.01
	3	553 (16.6)	238 (7.1)	
	≥ 4	595 (17.8)	143 (4.3)	
	Mean (SD)	2.3 (2.9)	0.9 (1.7)	
	Median	1	0	< 0.01
	Minimum	0	0	
	Maximum	39	20	
Hospitalizations	0	3,040 (91.0)	3,340 (100.0)	
	1	222 (6.6)	0 (0.0)	
	2	50 (1.5)	0 (0.0)	< 0.01
	3-4	24 (0.7)	0 (0.0)	
	≥ 5	4 (0.1)	0 (0.0)	
	Mean (SD)	0.1 (0.5)	0.0 (0.0)	
	Median	0	0	
	Minimum	0	0	
	Maximum	10	0	
Sick notes	0	2,614 (78.3)	2,907 (87.0)	
	1	269 (8.1)	263 (7.9)	
	2	143 (4.3)	79 (2.4)	< 0.01
	3-4	151 (4.5)	61 (1.8)	
	≥ 5	163 (4.9)	30 (0.9)	
	Mean (SD)	0.7 (1.8)	0.2 (0.9)	
	Median	0	0	< 0.01
	Minimum	0	0	
	Maximum	18	14	

*Unless otherwise indicated, all values represent number (%) of patients with each healthcare service over a 12-month period.
GAD: Generalized anxiety disorder; GP: General practitioner.

Discussion

We found that GAD patients in GP practices in Germany had higher levels of healthcare utilization than patients without anxiety or depression (matched on age and sex). They averaged twice as many GP visits than matched comparators, and 3.5 times as many physician-excused absences from work; they also had a higher prevalence of clinically recognized comorbidities. Results from our study are consistent with findings reported earlier from community surveys and primary care settings. One small (n = 219) survey-based study of Canadian patients who screened positive for GAD at community clinics averaged 5.3 medical visits annually versus 3.4 visits for other patients[22]. Two prior studies have reported a two-fold difference in visits to primary care physicians among GAD patients as compared with patients without GAD, irrespective of comorbid depression, but with similar sociodemographic characteristics and chronic physical conditions[20,23].

Forty percent of GAD patients did not receive psychotropic drugs from their GPs; only one-third received antidepressants (considered first-line therapy for GAD). Use of psychotropic medications was more common among women, and it increased with age. While levels of use of antidepressants are similar to those reported in previous studies[6,7], the high levels of use of benzodiazepines and analgesics noteworthy. One-third of patients in our study received benzodiazepines, and one in ten received other sedatives/hypnotics. In a 2000 survey of 558 primary care physicians in Germany, only 17% of patients with recognized GAD were reported to have received sedatives (presumably, mostly benzodiazepines)[6]. Whether this difference is an artifact of study design –our study was a retrospective analysis of computerized GP encounter data– while Wittchen's study was a cross-sectional survey of physicians –or represents a secular increase in the use of benzodiazepines and other sedatives is unknown. Use of NSAIDs (including COX-2 inhibitors) and opioids in our study appears to be quite high (40% and 8%, respectively); we know of no other study that has examined the use of these agents in patients with GAD.

The existence of an etiologic link between GAD and various comorbidities is an open issue at this time. On the one hand, it is possible that some of these conditions may be causally related to GAD. Stressful life events (e.g., death of a loved one, divorce, diagnosis of a serious medical condition) are known to be precipitating factors for GAD. It has been argued that increasing rates of GAD among persons aged >40 years may be suggestive of a common etiologic link between GAD and various chronic comorbidities. A diagnosis of GAD also may reflect typical patterns of worry about declining health associated with advancing age. However, it is also important to note that our findings may simply reflect opportunistic case-finding. Patients with GAD frequently have somatic complaints, and workups for such symptoms may increase the likelihood of clinical recognition of underlying (but unrelated) diseases. Caution should therefore be exercised in the interpretation of our findings.

Our database contained information on more than 1.2 million patients, 3340 of whom were found to have evidence of GAD during the study period. The estimated annual prevalence of GAD in our study (i.e., 0.3%) is markedly lower than the 2% reported in other studies[3,4]. The primary reason for this probably relates to the nature of the database, which only includes information recorded by GPs following patient encounters; patients who do not receive a GAD diagnosis from their GPs (irrespective

of whether or not they are known by their GPs to have GAD), or whose GAD is treated exclusively by specialists, would not be reflected in our count. We note, though, that the demographic characteristics of GAD patients in our study are similar to those reported in other studies (i.e., two-thirds women, three-quarters aged ≥ 40 years).

Almost thirty percent of GAD patients in our study also had been diagnosed with depression by their GPs, which is within the range (16-39%) reported in previous research[9,20]. The prevalence of digestive disorders, somatoform disorders, sleep disorders, and symptoms, signs, and ill-defined conditions also was high among GAD patients, consistent with earlier findings suggesting that GAD is commonly associated with various somatic disorders, including chest pain, irritable bowel syndrome, and heart disease[11,14,15,27-30].

Evidence-based guidelines recommend that selective serotonin receptor inhibitors (SSRIs), tricyclic antidepressants (TCAs), benzodiazepines, and venlafaxine be used for the treatment for GAD[31]. Many GAD patients in our study, however, had no record of receipt of such medications from their GPs. Patients in our study may have been prescribed such medications by specialists, however (the database only contains information on GP prescribing).

Some important limitations of our study should be noted. For one, information in the study database is limited to GP encounters. Given the high prevalence of comorbidities, it is reasonable to expect that GAD patients also had encounters with specialists. Furthermore, records of referrals, sick notes, and hospitalizations available in the study database are complete only to the extent that GPs recorded this information.

Study subjects were selected based on GP-recognized GAD, as evidenced by an encounter with an ICD-10 diagnosis code for this condition during the period of interest. Because we did not have access to patients' medical records, we cannot ascertain whether GPs used established DSM-IV criteria in rendering a diagnosis of GAD. Moreover, our database was limited to information on GP encounters. Thus, patients whose GAD was under the exclusive care of a specialist would not have been included in our GAD population –and in fact may have been selected for the comparison group if they saw their GP for other health problems. The degree to which any resulting misclassification in either or both patient groups impacted our findings is unknown.

In conclusion, our findings suggest that patients with GAD who are receiving care in GP settings in Germany have more clinically recognized comorbidities and higher levels of healthcare utilization than (age- and sex-matched) patients without evidence of anxiety or depression. Effective treatments for GAD may lead to reductions in healthcare utilization to the extent that these high levels may be attributable to this disorder. Further research is needed to better quantify the relationship between GAD and excess levels of healthcare utilization.

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